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| <b>Utility Patent Application</b> | <i>Attorney Docket No.</i>               | 3030-101          |
|                                   | <i>Appl. No.</i>                         | <b>10/506,893</b> |
|                                   | <i>Group</i>                             | 1647              |
|                                   | <i>First Inventor</i>                    | Eming             |
|                                   | <i>Proteolysis Resistant Active VEGF</i> |                   |

**CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10**  
(When using Express Mail, the Express Mail label number is **mandatory**;  
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Date: 12/06/2006

Joyce von Natzmer  
\_\_\_\_\_  
(type or print name of person certifying)



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of )  
)  
Eming et al. ) Att. Dkt.: **3030-101**  
)  
Appl. No.: 10/506,893 ) Examiner: Saoud, Christine J.  
)  
Filing date: March 6, 2003 ) Group Art Unit: 1647

For: ***PROTEOLYSIS RESISTANT ACTIVE VEGF***

**SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

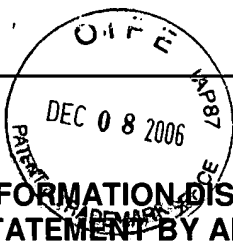
Under the provisions of 37 C.F.R. § 1.56, 1.97 and 1.98, applicants submits herewith references that were listed in the Information Disclosure Statement of August 31, 2005. In particular, a full copy of the references marked with an asterix are submitted herewith. These references were listed in the International Search Report, but have not been forwarded to the U.S. Patent and Trademark Office.

No fee is believed to be due. However, the Commissioner is authorized to charge deposit account no. 50-3135 as required for consideration of this submission.

Respectfully submitted,

/Joyce v. Natzmer/  
Joyce von Natzmer  
Registration No. 48,120  
Hall, Vande Sande & Pequignot, LLP  
**Customer No. 46002**

**December 6, 2006**



**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

*Complete if Known*

|                        |            |
|------------------------|------------|
| Application Number     | 10/506,893 |
| Nat. Phase Filing Date | 09/07/2004 |
| First Named Inventor   | Eming      |
| Group Art Unit         | NA         |
| Examiner Name          | NA         |

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|-------|---|--|---|------------------------|----------|
| Sheet | 1 |  | 3 | Attorney Docket Number | 3030-101 |
|-------|---|--|---|------------------------|----------|

**U.S. PATENT DOCUMENTS**

| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | U.S. Patent Document |                                      | Name of Patentee or Applicant<br>of Cited Document | Date of Publication<br>of Cited Document<br>MM-DD-YYYY |
|-----------------------|--------------------------|----------------------|--------------------------------------|--|--|
|                       |                          | Number               | Kind Code <sup>2</sup><br>(if known) |  |  |
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**FOREIGN PATENT DOCUMENTS**

| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Foreign Patent Document     |                     |                                 | Name of Patentee or Applicant of<br>Cited Document | Date of Publication of<br>Cited Document<br>MM-DD-YYYY | T <sup>6</sup> |
|-----------------------|--------------------------|-----------------------------|---------------------|---------------------------------|--|--|----------------|
|                       |                          | Office <sup>3</sup><br>Code | Number <sup>4</sup> | Kind <sup>5</sup><br>(if known) |  |  |                |
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Examiner  
Signature

Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code.

<sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached. AB indicates that only an English language abstract is attached.

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|  |                          |  |   | First Named Inventor     | Eming          |
|  |                          |  |   | Group Art Unit           | NA             |
|  |                          |  |   | Examiner Name            | NA             |
| Sheet  | 2                        | of   | 3 | Attorney Docket Number   | 3030-101       |
| <b>NON PATENT LITERATURE DOCUMENTS</b>                   |                          |  |   |                          |                |
| Examiner<br>Initials*                                    | Cite<br>No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published |   |                          | T <sup>2</sup> |
|  | 1                        | FRANK, S. ET AL, "Regulation of Vascular Endothelial Growth Factor Expression in Cultured Keratinocytes IMPLICATIONS FOR NORMAL AND IMPAIRED WOUND HEALING", JBC Online, Vol. 270, No. 21: 12607-12613 (May 26, 1995).   |   |                          |                |
|  | 2                        | FUKUMURA, D. ET AL, "Tumor Induction of VEGF Promoter Activity in Stromal Cells", Cell, Vol. 94: 715-725 (September 18, 1998).   |   |                          |                |
|  | 3                        | GOSPODAROWICZ, D. ET AL, "Isolation and characterization of a vascular endothelial cell mitogen produced by pituitary-derived folliculo stellate cells", Proc. Natl. Acad. Sci. USA, Vol. 86: 7311-7315 (October 1989).  |   |                          |                |
|  | 4                        | KECK, P. ET AL, "Vascular Permeability Factor, an Endothelial Cell Mitogen Related to PDGF", Science, Vol. 246: 1309-1312 (December 8, 1989).  |   |                          |                |
|  | 5                        | +KEYT, B. ET AL, "The Carboxyl-terminal Domain (111-165) of Vascular Endothelial Growth Factor Is Critical for Its Mitogenic Potency", The Journal of Biological Chemistry, Vol. 271, No. 13: 7788-7795 (March 29, 1996).                                      |   |                          |                |
|  | 6                        | +LAUER, G. ET AL, "Expression and Proteolysis of Vascular Endothelial Growth Factor is Increased in Chronic Wounds", The Journal of Investigative Dermatology, Vol. 115, No. 1: 12-18 (July 2000).   |   |                          |                |
|  | 7                        | *LAUER, G. ET AL, "Expression of the soluble variant of the vascular endothelial growth factor receptor Flt-1 in chronic wounds", Wound Repair and Regeneration, Vo. 8, No. 5 (September 2000).  |   |                          |                |
|  | 8                        | *LAUER, G. ET AL, "Generation of a novel proteolysis resistant vascular endothelial growth factor 165 variant by a site-directed mutation at the plasmin sensitive cleavage site", FEBS Lett., 531(2):309-13 (Nov. 6, 2002).                                   |   |                          |                |
|  | 9                        | *LAUER, G. ET AL, "VEGF expression chronic non-healing wounds", Archives of Dermatological Research, Vol. 293, No. 1-2, P145, page 79 (February 2001).   |   |                          |                |
|  | 10                       | LAWRENCE, W. ET AL, "Growth Factors in Wound Healing", Clinics in Dermatology, 12: 157-169 (1994).   |   |                          |                |
|  | 11                       | *MARKET, Y. ET AL, "Increased proteolytic resistance of ribonuclease A by protein engineering", Protein Engineering, England, Vol. 14, No. 10 (October 2001).  |   |                          |                |
|  | 12                       | MOHANRAJ, D. ET AL, "Expression of Biologically Active Human Vascular Endothelial Growth Factor in Yeast", Growth Factors, Vol. 12: 17-27 (1995).  |   |                          |                |
|  | 13                       | +NISSEN, N. ET AL, "Vascular Endothelial Growth Factor Mediates Angiogenic Activity during the Proliferative Phase of Wound Healing", American Journal of Pathology, Vol. 152, No. 6: 1445-1452 (June 1998).   |   |                          |                |
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<sup>1</sup>Unique citation designation number. <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

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|  | 14                       | POWERS, J.C. ET AL, "Proteases-structures, mechanism and inhibitors", NCBI abstract of Agents Actions Suppl., 42: 3-18 (1993) (Abstract).  |   |                          |                |
|  | 15                       | *Robinson, C. J. ET AL, "The splice variants of vascular endothelial growth factor (VEGF) and their receptors", Journal of cell Science, England, Vo. 114, No. Pt 5 (March 2001).  |   |                          |                |
|  | 16                       | SCHARFFETTER-KOCHANEK, K. ET AL, "Chronische Wunden und Wachstumsfaktoren Chronic wounds and growth factors", Zeitschrift für Hautkrankheiten, H&G, 11 (74): 664-672 (1999).   |   |                          | AB             |
|  | 17                       | SOKER, S. ET AL, "Neuropilin-1 Is Expressed by Endothelial and Tumor Cells as an Isoform-Specific Receptor for Vascular Endothelial Growth Factor", Cell, Vol. 92: 735-745 (March 20, 1998).   |   |                          |                |
|  | 18                       | *WU, X.C. ET AL, "Engineering of plasmin-resistant forms of streptokinase and their production in Bacillus subtilis: streptokinase with longer functional half-life", Appl Environ Microbiol., 64(3):824-9 (March 1998).                                       |   |                          |                |
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